Improved negative predictive value of EBUS-TBNA in isolated mediastinal / hilar lymphadenopathy:

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Results

A total of 100 patients underwent EBUS-TBNA for isolated mediastinal lymphadenopathy during the study period (Table 1) and the final diagnosis is demonstrated in Table 2.

Table 1: Patients’ Characteristics (n=100)

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>n=100</th>
<th>Sex (male) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity</td>
<td>70</td>
<td>28</td>
</tr>
<tr>
<td>African</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Symptoms:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Cough</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>- Haemoptysis</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>- Wheeze</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>- Chest pain</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>- Asymptomatic</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Patient characteristics stratified into diagnosis groups

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Eosinophilia</th>
<th>Lymphoma</th>
<th>Tuberculosis</th>
<th>Sarcoidosis</th>
<th>Carcinoma</th>
<th>Reactive lymphadenopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-20</td>
<td>0</td>
<td>6 (12%)</td>
<td>0</td>
<td>3 (15%)</td>
<td>16 (89%)</td>
<td>5 (11%)</td>
</tr>
<tr>
<td>21-40</td>
<td>16 (89%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6 (12%)</td>
</tr>
<tr>
<td>41-60</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>&gt;60</td>
<td>0</td>
<td>0</td>
<td>4 (8%)</td>
<td>0</td>
<td>0</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Granulomatous disorders

Sarcoidosis accounted for 20% of the final diagnoses. The sensitivity of EBUS-TBNA was 95% (36/38 correctly diagnosed).

Malignant diagnoses

Lymphoma accounted for 5% of the diagnoses. EBUS-TBNA correctly diagnosed 20 patients (sensitivity 93.3%). 6/4 (41%) of patients had extra-thoracic lymphadenopathy (nodes included: abdomen, mediastinum, neck, 1,inguinal 1). One patient had previously undergone a left thoracotomy; therefore he was immunosuppressed.

Conclusions

In patients undergoing EBUS-TBNA at our centre for isolated mediastinal lymphadenopathy (and if hilar lymphadenopathy is present in ≤3 station), EBUS-TBNA correctly diagnosed 61% of reactive lymphadenopathy rather than one of the traditional malignant diagnoses (bronchitis, tuberculosis, lymphoma, carcinoma).

Clinical and radiological features that suggest a high probability index for reactive lymphadenopathy may aid in deciding whether or not the need for further sampling in cases of negative EBUS-TBNA exists.

- ≥3 lymph stations enlarged with symmetrical mediastinal and hilar lymphadenopathy (suggestive of sarcoidosis);

- lung parenchymal abnormalities (upper lobe involvement in sarcoidosis and upper zone nodularity in sarcoidosis);

- non-Caucasian ethnicity (suggestive of tuberculosis);

- evidence of additional extrathoracic lymphadenopathy (lymphoma or carcinoma),

- chronic cough/lymphadenopathy (suggestive of sarcoidosis or lymphoma),

- pleurisy (suggestive of sarcoidosis or lymphoma),

- absence of disease associated with lymphadenopathy.

With the increasing use of CT, MRI, echocardiography and the increasing prevalence of chronic diseases, the diagnosis of reactive lymphadenopathy is becoming more frequent and reactive lymphadenopathy is representing a higher proportion of these diagnoses.

The negative predictive value of EBUS-TBNA may be significantly higher than previously reported due to this subgroup of patients. This may allow a period of surveillance rather than requiring further invasive sampling with medically-supervised follow up.

Materials and Methods

The study was a prospective observational cohort of all patients undergoing EBUS-TBNA for investigation of isolated mediastinal and/or hilar lymphadenopathy, between March 2010 and November 2012, at the North West Lung Centre, University Hospital of South Manchester, UK. Patients were included if they had enlarged hilar or mediastinal lymph nodes (≥10 mm in short axis diameter) without evidence of an intrathoracic mass and no evidence of extra-thoracic metastatic disease. The diagnosis for each patient was based on EBUS-TBNA results, any subsequent pathological sampling and clinical-radiological follow-up, which was undertaken for a period of six months after the investigation, based on EBUS-TBNA results, any subsequent pathological sampling and clinical-radiological follow-up failed to demonstrate any evidence of the other diagnoses.

Introduction

The traditional differential diagnosis of isolated mediastinal and hilar lymphadenopathy includes benign granulomatous diseases such as sarcoidosis and tuberculosis and malignant conditions such as lymphoma and carcinoma. Each of these diagnoses may require different management and treatment. Lymphadenopathy in which such causes have been excluded has been termed ‘reactive lymphadenopathy’. In a prospective trial of 77 patients with isolated mediastinal lymphadenopathy EBUS-TBNA predicted mediastinal malignancy in 89% of patients (based on EBUS-TBNA results, any subsequent pathological sampling and clinical-radiological follow-up) with a negative predictive value of 52%. EBUS-TBNA is therefore recommended as a first line investigation in such patients. However the negative predictive value was 40% suggesting in cases of negative EBUS-TBNA further sampling, such as mediastinoscopy, is required. Of note, only 4 patients in this study were ultimately diagnosed with ‘reactive lymphadenopathy’.

There is increasing evidence that common chronic diseases, both respiratory and non-respiratory, are associated with mediastinal and hilar lymphadenopathy. This includes: emphysema and chronic bronchitis, interstitial lung disease, bronchiectasis, pulmonary hypertension, heart failure and rheumatoid arthritis. Lymphadenopathy in this condition would fall under the term ‘reactive lymph nodules’ following pathological sampling. Could this lead to a higher prevalence of reactive lymphadenopathy in isolated lymphadenopathy, requiring these patients require further surgical biopsy following a negative EBUS-TBNA? 

The overall objective of this study was to determine the prevalence of reactive lymphadenopathy in patients undergoing EBUS-TBNA for isolated lymphadenopathy at our centre. Secondary aims were to determine the presence of reactive and non-reactive lymphadenopathy which may explain the lymphadenopathy in this group and to investigate for potential clinical and radiological features that could identify which patients may need further invasive sampling which may undergo surveillance in cases of negative EBUS-TBNA.

Materials and Methods

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Diagnoses were classified as one of sarcoidosis, tuberculosis, lymphoma, carcinoma or reactive lymphadenopathy. A lymph node was only classified as reactive if the EBUS-TBNA, any subsequent pathological sampling and 6 months of clinical-radiological follow-up failed to demonstrate any evidence of the other diagnoses.